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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/522,716	03/10/2000	Edward P. Cohen	07411.0005.NPUS00	6035

7590 01/26/2006

ATT: IP PROSECUTION
HOWREY, SIMON, ARNOLD & WHITE, LLP
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EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/522,716	COHEN, EDWARD P.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 41-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 41-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/14/2005 has been entered.

2. Applicant's response and amendment to the claims received on 11/14/2005 is acknowledged.

3. Claims 26 and 41-54, are pending.

Claims 26 and 47 are amended.

Claims 26 and 41-54, are examined on the merits.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections – 35 U.S.C. § 112

5. The rejection of Claims 47-53 under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure for "preventing tumor reccurence" is withdrawn due to Applicant's amendment to claim 47 which now reads "inhibiting tumor cell growth".

Claim Rejections – 35 U.S.C. § 102(b)

6. The rejection of Claims 26, 41, 42, and 44-45 under 35 U.S.C. § 102(b) as being anticipated by Eisenbach et al. (EP 0569678A2) is withdrawn due to Applicant's amendment to the claims "wherein said antigen-presenting cell is selected from the group consisting of professional antigen-presenting cells and facultative antigen-presenting cells". Applicant's arguments that tumor cells of Eisenbach are neither professional nor facultative antigen presenting cells are found to be persuasive.

Claim Rejections – 35 U.S.C. § 102(e)

7. The rejection of Claims 26, 41, 42, and 44-45 under 35 U.S.C. § 102(e) as being anticipated by Eisenbach et al. (EP 0569678A2) is withdrawn due to Applicant's amendment to the claims "wherein said antigen-presenting cell is selected from the group consisting of professional antigen-presenting cells and facultative antigen-presenting cells". Applicant's arguments that tumor cells of

Eisenbach are neither professional nor facultative antigen presenting cells are found to be persuasive.

Maintained and New Grounds of Rejection

Claim Rejections – 35 U.S.C. § 112, 1st paragraph

8. The rejection of Claims 26, 41-46, and 54, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.** The claims have been amended to recite "total genomic DNA" as a limitation, however, the addition of the term "total" does not find support in the specification as filed. The applicant points to pages 30-32 for support of the term, however upon review of the specification no support for the term "total" is found. The broadest reasonably interpretation of the term genomic DNA includes a single gene with all its introns and exons. The specification at pages 30-32 only provides support for the broad genus of the term "genomic DNA" and no contemplation of the species "total genomic DNA" has been disclosed. Applicant is invited to specifically point out and disclose support for this term.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 26 and 41-54 are rejected under 35 U.S.C. §103(a) as being unpatentable over Schmidt et al. (U.S. Patent Publication 2002/0085997; effective filing date November 21, 1996) in view of Sun T et al. (Cancer Gene Ther. 2(3): 183-190, 1995) and Hiserodt et al. (U.S. Patent 6,277,368; effective filing date October 29, 1996 and patented on August 21, 2001).

The instant claims are drawn to a method of treating a tumor in an animal which comprises administering to an animal an antigen-presenting cells that expresses at least one class I MHC or class II MHC determinant that is syngeneic to said animal and at least one class I MHC or class II MHC determinant that is allogeneic to the animal wherein the antigen-presenting cells are either professional or facultative antigen-presenting cells transfected with genomic DNA isolated from the tumor cells of said animal. Claims 41 and 42 provide the additional method step of transfecting the antigen-presenting cells with a nucleic acid molecule that codes for at least one cytokine. Claim 43 further limits the antigen-presenting cell to fibroblasts, macrophages, B cells, or dendritic cells. Claims 45 and 46 provide the limitation that the tumor is a solid tumor or hematological tumor. Claim 46 recites the method wherein the animal is a human subject. Claim 47 is drawn to a method of inhibiting tumor cell growth in an animal which comprises administering to an animal an antigen-presenting cells that expresses at least one class I MHC or class II MHC determinant that is syngeneic to said animal and at least one class I MHC or class II MHC determinant that is allogeneic to the animal wherein the antigen-presenting cells are either professional or facultative antigen-presenting cells transfected with

genomic DNA isolated from the tumor cells of said animal. Claims 48 and 49 provide the additional method step of transfecting the antigen-presenting cells with a nucleic acid molecule that codes for at least one cytokine. Claim 50 further limits the antigen-presenting cell to fibroblasts, macrophages, B cells, or dendritic cells. Claims 51 and 52 provide the limitation that the tumor is a solid tumor or hematological tumor. Claim 53 recites the method wherein the animal is a human subject. Finally, claim 54 recites the method of claim 26 wherein the genomic DNA is sheared.

Schmidt et al. teach a method of treating tumors by administering a composition that contains tumor cells at least some of which contain at least one MHC-I haplotype of the patient on the cells surface and which are charged with one or more peptides binding to the MHC-I molecule in such a way that the tumor cells are recognized as foreign by the patient's immune system in context with peptides and trigger a cellular immune response, see Abstract, lines 1-8. Schmidt et al. teach treating a patient with a tumor using autologous and/or allogeneic tumor cells and antigen-presenting cells, such as fibroblasts, transfected with cytokine genes, see pages 5 and 6, paragraph 65. One example of an expressed cytokine is IL-2, see page 6, paragraph 65. Autologous cells (cells native to the patient) contain MHC determinants that are syngeneic to the patient (genetically compatible for transplant purposes: having an identical or closely similar genetic makeup, especially one that will allow the transplantation of tissue without provoking an immune response).

Schmidt et al. further teach that instead of tumor cells, autologous fibroblasts, or fibroblasts cell lines which are either matched to the HLA-subtype of the patient or have been transfected with the corresponding MHC-I gene may be "charged" by the process according to the invention with one or more peptides derived from tumor antigens expressed by the tumor cells of the patients, see page 7, paragraph 85. Schmidt et al. also teach that instead of fibroblasts, dendritic cells (antigen presenting cells of the skin) can be isolated from the patient and mixed with peptides derived from tumor antigens that bind to MHC-I or an MHC-II molecules of the patient, see page 7, paragraph 86, lines 1-8. Schmidt et al. further disclose the method wherein the tumor is a melanoma, see page 8, Example 2, paragraph 109.

Schmidt et al. do not teach transfecting antigen-presenting cells with genomic DNA or sheared genomic DNA from a neoplasm such that some gene products represent tumor-associated T-cell epitopes. This deficiency is made up for in the teachings of Sun et al.

Sun et al. teach cytokine-secreting fibroblasts transfected with sheared, unfractionated genomic DNA from different mouse neoplasms as a method to induce an antitumor immune response in the animal, see page183, right column, first complete paragraph lines 1-3, and the bridging sentence between pages 183 and 184. Sun et al. also teach that co-expression of allogeneic antigens augmented the cells' immunogenic properties as it protected the recipients against the growth of the modified cells, see page 189, right column, second complete paragraph, last sentence.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Schmidt et al. and Sun et al. for the purpose of generating a composition that induces an enhanced antitumor response in the animal in need thereof by using the peptides or genomic DNA from the tumor to stimulate T cells that specifically recognize the tumor cells.

Neither Schmidt et al. nor Sun et al. teach a method of cancer immunotherapy wherein the subjects are human. This deficiency is made up for in the teachings of Hiserodt et al.

Hiserodt et al. teach development of a cellular composition and method for using it in cancer immunotherapy, particularly in human patients, see Abstract, lines 1-3.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Schmidt et al. and Sun et al. for the purpose of generating a composition that induces an enhanced antitumor response in a human since Hiserodt et al. teach that cancer remains a leading cause of death throughout the world, see column 1, Background, lines 23-25. Hiserodt et al. further teach that many solid tumors are resistant to other approaches such as surgery, radiotherapy and general chemotherapy, see column 1, Background, lines 25-31.

One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Schmidt et al., Sun et al., and Hiserodt et al. since Sun et al. teach that cytokine secreting

antigen-presenting cells transfected with genomic DNA from neoplasms induce tumor-specific immune responses that prolong the lives of tumor-bearing animals, see page 183, title and Abstract. Sun et al. further teach that their data raise the possibility that a cell line altered previously for cytokine secretion (fibroblasts that are allogeneic to the tumor-afflicted animal) may be readily modified to provide immunologic specificity for the neoplasms of individual cancer patients, see Sun et al., page 183, Abstract, last sentence.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Humphrey, Ph.D.
January 20, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER